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SUBJECT

Study Report on:

Strontium Metabolism in the Rebuilding of Skeletal Tissue

This report describes the relationship between calcium and strontium in bone metabolism. Whole body comparisons in the form of balance studies, plasma kinetics, and biochemical bone differences are briefly reviewed. The value of strontium as a qualitative calcium mimetic is established. A procedure of strontium deposition in the bones is presented as a means to study postflight bone rebuilding and to locate areas of inflight demineralization.

S. N. Brand

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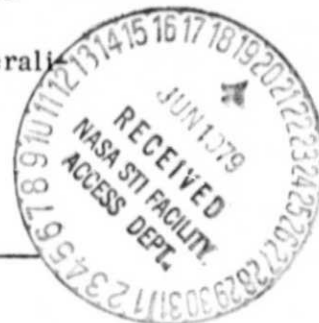
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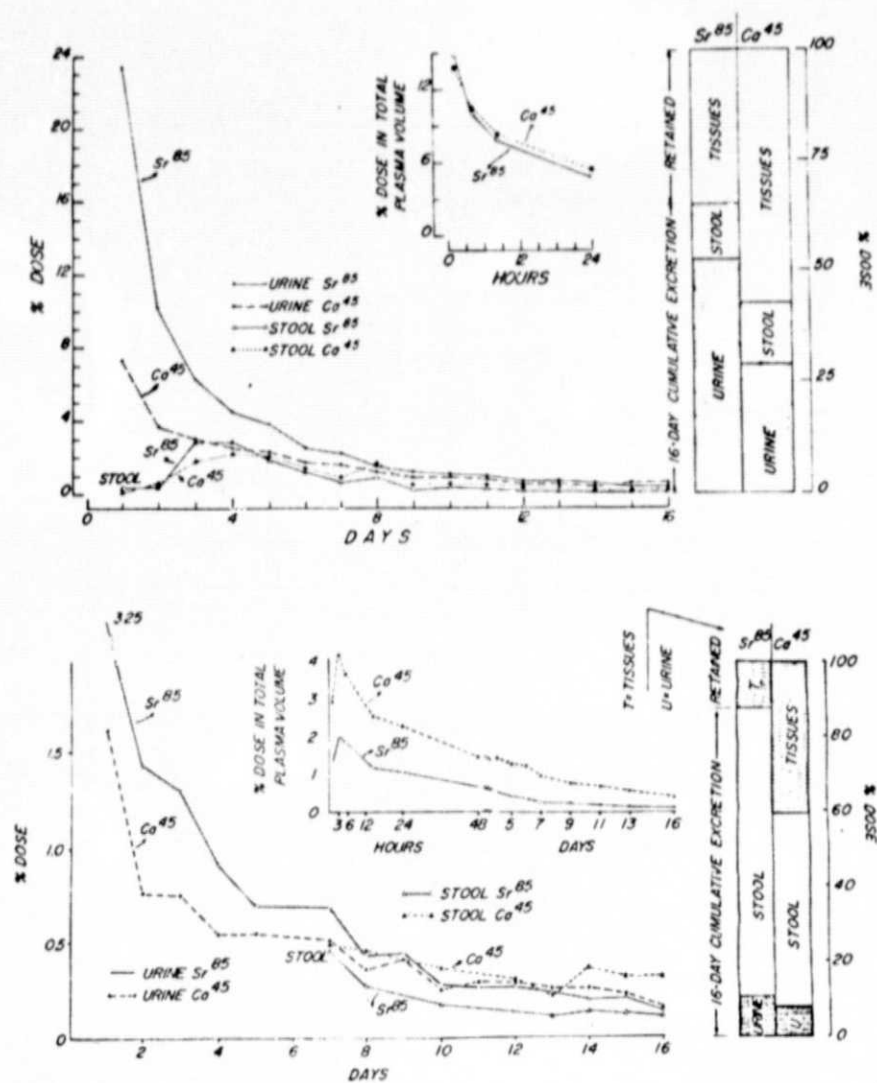J. Waligora

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ASD 4028

STRONTIUM METABOLISM IN THE REBUILDING
OF SKELETAL TISSUE

Bone density studies on the crewmen of the Skylab 3 and 4 missions showed varying degrees of bone mineral loss upon exposure to a weightless environment. Baylink and Holton[1] demonstrated in rats that the mineral loss may be due to a cessation of bone formation and that postflight bone formation increased dramatically to correct the defect in a relatively short period of time. Operating on the idea of a rapid postflight rebuilding of bone, Palmer and Karagianes[2] sought to measure the rate of bone mineral uptake following immobilization with the use of a radioactive bone mineral tracer, strontium 85 (^{85}Sr). ^{85}Sr is a pure gamma emitter with a half-life of 65 days. These characteristics make it well suited for external counting techniques. It is used in lieu of the calcium isotopes because the calcium isotopes cannot penetrate the tissue depth or have too short of a half-life for adequate study.

Evidence of the relationship between strontium and calcium kinetics has been most extensively studied by Spencer. Oral doses of ^{85}Sr and ^{45}Ca result in high fecal and low urinary levels of both tracers.[3,4] Intravenous injections of the strontium and calcium yield high urinary and low fecal levels of both tracers.[3] In every case the amount of strontium is higher than that of calcium with the level being 20 to 30% higher in fecal samples of oral doses, and approximately 15% higher in urine samples of intravenous doses.[3] The conclusions drawn from these studies are that, 1) strontium is not absorbed by the gastrointestinal tract as well as calcium, and 2) it is excreted in higher quantities than calcium by the kidney. The result is a significantly lower concentration of strontium in the tissues of the body, especially under oral administration. The strontium that enters the body, though, appears to have the same plasma kinetics as calcium (Figure 1 and 2). To further examine strontium and plasma kinetics, chemical agents modifying the tracer excretion rates were studied.

Fig. 1.—Metabolism of an Intravenous dose of Sr[85] and Ca[45]. Both tracers were injected simultaneously.

Fig. 2.—Metabolism of orally-administered Sr[85] and Ca[45] in man. Both tracers were given simultaneously.

From Reference 3.

The removal of strontium and calcium in men under both short and long term exposure periods was examined using high and low levels of calcium, strontium, ammonium chloride, and magnesium. The removal of radiostrontium from the body, immediately upon exposure, is basically removal from the blood via the kidneys. The agents effect the removal at the site of the kidney itself. This is evidenced by the differing patterns of calcium and strontium urinary excretions and the lack of differences in fecal and plasma levels from control.[5,6,7] The removal of radiostrontium two or more weeks after exposure is believed to be removal from the bone. The calcium dietary intake showed little to no effect upon calcium and strontium excretion.[7] A low calcium dietary intake in conjunction with ammonium chloride, though, produces increased and identical patterns of calcium and strontium urinary excretion.[6,7] Magnesium, calcium,[5] and strontium[8] infusions also result in similar and higher losses of calcium and strontium excretion. These results indicate that with exception of the GIT and kidney, calcium and strontium metabolism are very similar.

Since calcium is mainly a bone mineral, the site of strontium activity would also be expected to be at the bone. Strontium has been used as a calcium mimetic to study skeletal metabolism, both for research[9,10] and clinical purposes.[11,12] Direct examinations of strontium metabolism upon bone show that lanthanum, an inhibitor of calcium deposition, is also an inhibitor of strontiumdeposition.[13] Vitamin D has similar effects on strontium and calcium in the deposition of the minerals in bone.[14] Calcium content was higher than strontium in the tibia of the rat by about 30%, but strontium and calcium plasma concentrations were found to be equivalent. This indicates that there may be a discrimination at the site of the bone as well, but that the discrimination is not so great as to effect plasma concentrations. The discrimination appears to be a function of size differences between the strontium and the calcium in the crystallization of hydroxyapatite.[15] In the amorphous stage of bone formation

strontium is readily incorporated into the bone, but as crystallization occurs, the larger strontium is eliminated and replaced by the calcium. Strontium deposition, therefore, will yield a qualitative measurement of the distribution of bone mineral loss and the proportionality of those losses as they are distinguished throughout the body by the rebuilding of the demineralized bone.

Procedure

The experimental plan is based upon a preflight and a postflight comparison of the accumulation of ^{85}Sr as detected by the whole-body counter located in the Low Level Radiation Counting Laboratory at JSC. The laboratory contains the lowest level of radioactive background in the free world. A preflight, or control, study will begin at least 5 weeks before the flight while the experimental study will start the first day postflight. Immediately prior to the beginning of the postflight experiment, a whole-body scan and a plasma sample will be taken to measure pre-existing ^{85}Sr counts and concentrations in the body.

The preflight study will require a 1.0 μCi/kg body weight dose of ^{85}Sr to be injected intravenously. Plasma samples of 2.0 mls will be collected 30 minutes after the injection and every 72 hours thereafter, in the morning while the subject is in the post-absorptive state. The ^{85}Sr becomes distributed in the body and initially falls rapidly in concentration. The purpose of the plasma sampling is to maintain a measure of the ^{85}Sr distributed throughout the body fluids. Plasma radio-activity will be measured by a scintillation counter and will be recorded in terms of percent administered dose.

Immediately following the collection of plasma samples, a whole-body scan using a whole-body counter will measure the number of radioactive counts and the location of the counts in the body. The readings will be taken at an energy range of 0.44 to 0.58 MeV, 0.51 MeV being the preferred value. As the time following injection increases the amount of ^{85}Sr in the body fluids will decrease rapidly while the amount localized in the bones will stabilize or

decrease gradually.   Two phases of mineral metabolism will be occurring. One, and the more rapid of the two, is surface activity, a rapid exchange of the isotope in plasma with bone. The second, of which this study concerns itself with, is the focal uptake of ^{85}Sr in areas of new bone formation. Surface activity occurs mainly in the early phase and appears to have little influence by 7 days. By around 7 days the tracer is largely incorporated into areas of new bone formation,[16] probably as amorphous bone, then crystallized bone. Therefore, in the preflight analysis, a qualitative measurement of bone formation will be derived during a given period of time.

The measurements will be taken for a period of 16 days as previously described.   An estimation of bone formation rate will be determined from a graph showing the relative bone and plasma activity levels as a function of time. The value will be in terms of the percent administered dose located in the bone (at a specific site or as a whole) at a particular elapsed time period. The time period chosen will depend upon the values of the body counts and plasma counts, probably around 7 days post injection.

The same procedures will be followed in the postflight experiment. Because of the expected jump in bone formation activity at the site of demineralization, a rapid and large uptake of ^{85}Sr should occur at those sites. They should be distinct by around the 7th day after the injection. The results should manifest themselves as localized areas of higher specific activity, higher number of ^{85}Sr counts, and consequently a higher estimation of bone formation rate when compared to the preflight values. A comparison of the pre- and postflight areas of localized specific activity should also give an indication of the type of bone that is demineralized during exposure to zero-g. Of particular interest is the resolution of whether demineralization occurs in high stress related bones, throughout the body, or only in leg bones. This type of information will be instrumental in directing the theories and type of research to be followed in the future.

Fundamental to the study then are the assumptions that the ^{85}Sr will be distributed evenly throughout the body, that all areas of bone will be equally exposed to the ^{85}Sr so that an equal opportunity of ^{85}Sr deposition will be available to all sites undergoing rebuilding, and that those whole-body scans considered to have negligible plasma counts will be interpreted as ^{85}Sr bone contents.

Under the procedures outlined above, the calculated, strontium radiation dose to an adult human would be 88 mrem to the skeleton and 46 mrem to the whole-body. A single μCi injection of ^{85}Sr would be approximately 44 mrem and 23 mrem, respectively.[2] Such doses are well below the recommended maximum radiation exposure levels for experimental subjects.[17]

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